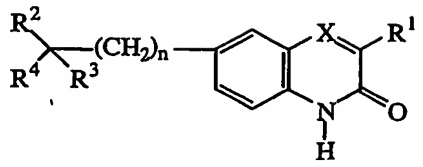
CLAIMS

1. A compound of formula (I),



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR^5, wherein R^5 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thienyl;

R^2 is hydrogen or hydroxy or taken together with R^3 or R^4 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^6R^7$	(a-1),
-O-H	(a-2),
$-O-R^8$	(a-3),
$-S-R^9$	(a-4), or
$-C\equiv N$	(a-5),

wherein

s is 0, 1, 2 or 3;

R^6 is –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thienylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl;

R^7 is hydrogen or C_{1-6}alkyl;

R^8 is C_{1-6}alkyl, C_{1-6}alkylcarbonyl or di(C_{1-6}alkyl)aminoC_{1-6}alkyl; and

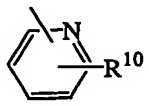
R^9 is di(C_{1-6}alkyl)aminoC_{1-6}alkyl;

or R^3 is a group of formula

-Z- (b-1),

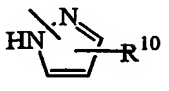
wherein

Z is a heterocyclic ring system selected from

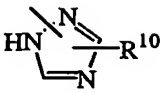


(c-1)

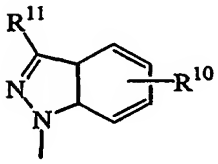
(c-2)



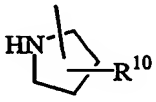
(c-3)



(c-4)

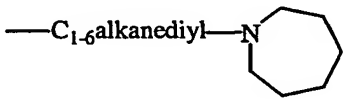


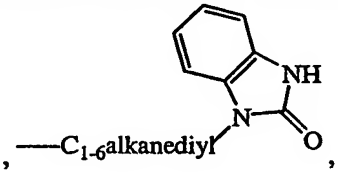
(c-5)



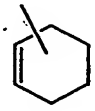
(c-6)

wherein each R^{10} independently is hydrogen, C_{1-6}alkyl, aminocarbonyl, hydroxy,





C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, morpholino, C_{1-6}alkylimidazolyl, or pyridinylC_{1-6}alkylamino;

R^4 is hydrogen, C_{1-6}alkyl, furanyl, pyridinyl, arylC_{1-6}alkyl or  ;

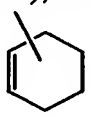
aryl is phenyl or phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy;

with the proviso that when

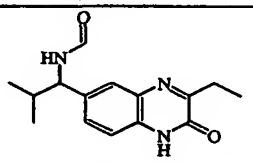
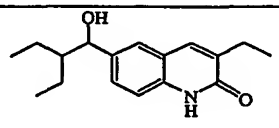
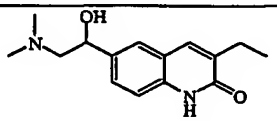
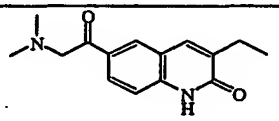
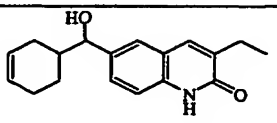
n is 0, X is N, R^2 is hydrogen, R^3 is a group of formula (b-1), Z is the heterocyclic ring system (c-2) or (c-4) wherein said heterocyclic ring system Z is attached to the rest of the molecule with a nitrogen atom, and R^{10} is hydrogen; then

R^4 is other than C_{1-6}alkyl or pyridinyl.

2. A compound as claimed in claim 1 wherein
n is 0 or 1; X is N or CR^5, wherein R^5 is hydrogen; R^3 is a radical selected from (a-1), (a-2) or (a-3) or is a group of formula (b-1) i.e. –Z-; s is 0, 1 or 2; R^6 is –CHO, C_{1-6}alkyl, piperidinylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl; R^8 is C_{1-6}alkyl; when R^3 is a group of formula (b-1) then Z is a heterocyclic ring system selected from (c-2) or (c-4); and each R^{10} independently is hydrogen, C_{1-6}alkyl or C_{1-6}alkyloxyC_{1-6}alkylamino.

3. A compound according to claim 1 and 2 wherein
n is 0; X is N or CR^5, wherein R^5 is hydrogen; R^1 is C_{1-6}alkyl; R^2 is hydrogen or hydroxy or taken together with R^4 may form =O; R^3 is a radical selected from (a-1) or (a-2); s is 0 or 1; R^6 is –CHO or C_{1-6}alkyl; and R^4 is hydrogen, C_{1-6}alkyl or  .

4. A compound according to claim 1, 2 and 3 wherein the compound is selected from compound No 1, compound No 5, compound No 7, compound No 3 and compound No 17.

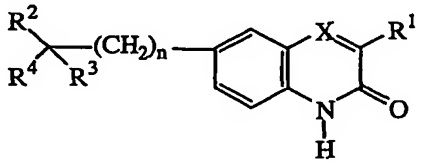
 compound 1	 compound 5
 compound 7	 compound 3
 compound 17	

5. A compound as claimed in any of claims 1 to 4 for use as a medicine.

6. A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in claim 1 to 4.

7. A process of preparing a pharmaceutical composition as claimed in claim 6 wherein the pharmaceutically acceptable carriers and a compound as claimed in claim 1 to 4 are intimately mixed.

8. Use of a compound for the manufacture of a medicament for the treatment of a PARP mediated disorder, wherein said compound is a compound of formula (I)



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

n is 0, 1 or 2;

X is N or CR^5, wherein R^5 is hydrogen or taken together with R^1 may form a bivalent radical of formula -CH=CH-CH=CH-;

R^1 is C_{1-6}alkyl or thienyl;

R^2 is hydrogen or hydroxy or taken together with R^3 or R^4 may form =O;

R^3 is a radical selected from

$-(CH_2)_s-NR^6R^7$ (a-1),
-O-H (a-2),
$-O-R^8$ (a-3),
$-S-R^9$ (a-4), or
—C≡N (a-5),

wherein
s is 0, 1, 2 or 3;
R^6 is –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thienylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl;
R^7 is hydrogen or C_{1-6}alkyl;
R^8 is C_{1-6}alkyl, C_{1-6}alkylcarbonyl or di(C_{1-6}alkyl)aminoC_{1-6}alkyl; and

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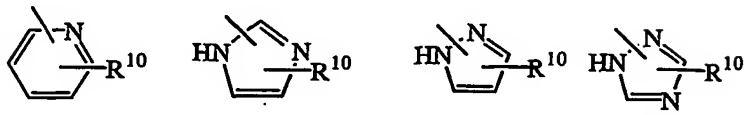
or R^3 is a group of formula

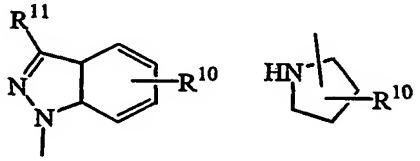
-Z- (b-1),

wherein

Z is a heterocyclic ring system selected from

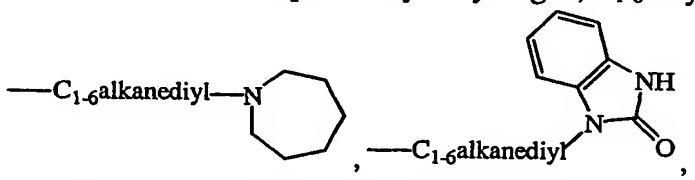


(c-1) (c-2) (c-3) (c-4)

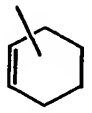


(c-5) (c-6)

wherein each R^{10} independently is hydrogen, C_{1-6}alkyl, aminocarbonyl, hydroxy,



C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, morpholino, C_{1-6}alkylimidazolyl, or pyridinylC_{1-6}alkylamino;

R^4 is hydrogen, C_{1-6}alkyl, furanyl, pyridinyl, arylC_{1-6}alkyl or  ;

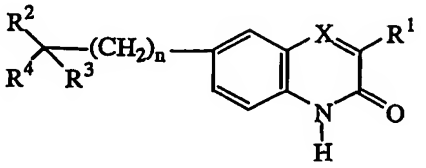
aryl is phenyl or phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

9. Use according to claim 8 of a PARP inhibitor of formula (I) for the manufacture of a medicament for the treatment of a PARP-1 mediated disorder

10. Use according to claim 8 and 9 wherein the treatment involves chemosensitization.

11. Use according to claim 8 and 9 wherein the treatment involves radiosensitization.

12. A combination of a compound with a chemotherapeutic agent wherein said compound is a compound of formula (I)



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$-S-R^9$	(a-4), or
$-C\equiv N$	(a-5),

wherein

s is 0, 1, 2 or 3;

R^6 is –CHO, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkylcarbonylaminoC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, piperidinyl, piperidinylC_{1-6}alkyl, piperidinylC_{1-6}alkylaminocarbonyl, C_{1-6}alkyloxy, thienylC_{1-6}alkyl, pyrrolylC_{1-6}alkyl, arylC_{1-6}alkylpiperidinyl, arylcarbonylC_{1-6}alkyl, arylcarbonylpiperidinylC_{1-6}alkyl, haloindozolylpiperidinylC_{1-6}alkyl, or arylC_{1-6}alkyl(C_{1-6}alkyl)aminoC_{1-6}alkyl;

R^7 is hydrogen or C_{1-6}alkyl;

R^8 is C_{1-6}alkyl, C_{1-6}alkylcarbonyl or di(C_{1-6}alkyl)aminoC_{1-6}alkyl; and

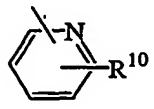
R^9 is di(C_{1-6}alkyl)aminoC_{1-6}alkyl;

or R^3 is a group of formula

-Z- (b-1),

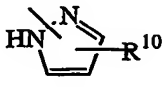
wherein

Z is a heterocyclic ring system selected from

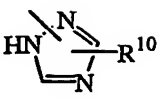


(c-1)

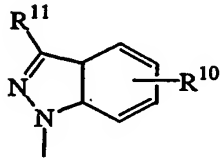
(c-2)



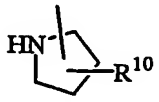
(c-3)



(c-4)

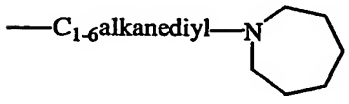


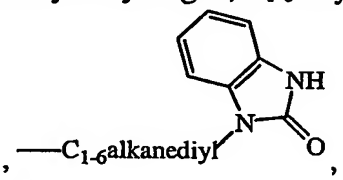
(c-5)



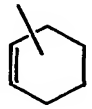
(c-6)

wherein each R^{10} independently is hydrogen, C_{1-6}alkyl, aminocarbonyl, hydroxy,





C_{1-6}alkyloxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkylamino, arylC_{1-6}alkyl, di(phenylC_{2-6}alkenyl), piperidinylC_{1-6}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkylC_{1-6}alkyl, aryloxy(hydroxy)C_{1-6}alkyl, haloindazolyl, arylC_{1-6}alkyl, arylC_{2-6}alkenyl, morpholino, C_{1-6}alkylimidazolyl, or pyridinylC_{1-6}alkylamino;

R^4 is hydrogen, C_{1-6}alkyl, furanyl, pyridinyl, arylC_{1-6}alkyl or  ;

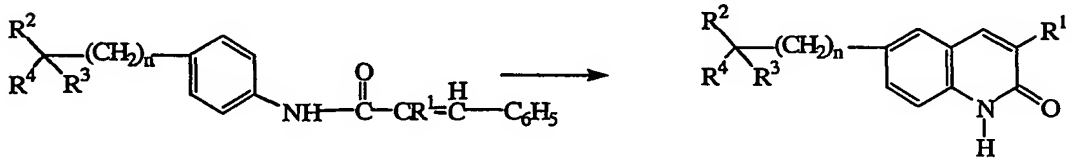
aryl is phenyl or phenyl substituted with halo, C_{1-6}alkyl or C_{1-6}alkyloxy.

13. A process for preparing a compound as claimed in claim 1, characterized by

a) the hydrolysis of intermediates of formula (VIII), according to art-known methods, by submitting the intermediates of formula (VIII) to appropriate reagents, such as, tinchloride, acetic acid and hydrochloric acid, in the presence of a reaction inert solvent, e.g. tetrahydrofuran.

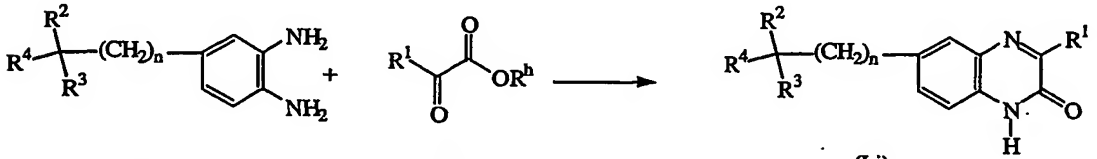
(VIII) (I)

b) the cyclization of intermediates of formula (X), according to art-known cyclizing procedures into compounds of formula (I) wherein X is CH herein referred to as compounds of formula (I-j), preferably in the presence of a suitable Lewis Acid, e.g. aluminum chloride either neat or in a suitable solvent such as, for example, an aromatic hydrocarbon, e.g. benzene, chlorobenzene, methylbenzene and the like; halogenated hydrocarbons, e.g. trichloromethane, tetrachloromethane and the like; an ether, e.g. tetrahydrofuran, 1,4-dioxane and the like or mixtures of such solvents.



(X) (I-j)

c) the condensation of an appropriate ortho-benzenediamine of formula (XI) with an ester of formula (XII) wherein R^h is C_{1-6}alkyl, into compounds of formula (I), wherein X is N, herein referred to as compounds of formula (I-i), in the presence of a carboxylic acid, e.g. acetic acid and the like, a mineral acid such as, for example hydrochloric acid, sulfuric acid, or a sulfonic acid such as, for example, methanesulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfonic acid and the like.



(XI) (XII) (I-i)